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(54) Title: POLYURETHANE-COATED INTRAVASCULAR PROSTHESES (STENTS) FOR THE TREATMENT OF BLOOD VESSEL STENOSIS

(57) Abstract

A new method to treat blood vessel stenosis using endovascular prostheses which are coated with amphiphilic polyurethanes to which medicines can be coupled. By coating endovascular prosthesis with amphiphilic polyurethanes, we have succeeded in significantly improving the bio- and bloodcompatibility of endovascular prostheses. These amphiphilic polyurethanes have the property, when implanted in human or animal tissue and blood vessels, of remaining stable and seeming not to provoke an inflammatory reaction. Furthermore it is possible to incorporate medicines in these polymers which, after implantation of the polymers, are slowly released at the location of the place of implantation. This system can further reduce the thrombogenicity of the prostheses coated with the polyurethanes and inhibit the rejection against these prostheses.

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POLYURETHANE-COATED INTRAVASCULAR PROTHESES (STENTS) FOR THE TREATMENT OF BLOOD VESSEL STENOSES. A new method to treat blood vessel stenoses by means of endovascular protheses which are coated with amphiphylic polyurethanes to which medicines can be coupled.

DESCRIPTION

Treatment of blood vessel stenoses by means of a balloon catheter is a popular method. Last year, more than 6,000 patients with coronary heart disease were treated by this method in our country. The problem with this method is on the one hand the danger that a tear occurs during the blowing up of the balloon whereby the blood vessel can close and thus cause an acute myocardial infarction, on the other hand it is well documented that this treatment method is accompanied by a frequent restenosis of the treated blood vessel within 6 months of the treatment. To solve this problems, medicines were tested in order to prevent the restenosis and furthermore new devices were developed. One of these new methods consist of placing a metal intravascular prothesis (stent) at the level of the vessel stenosis. This method is very efficient for treating vessel tears which can occur during balloon dilatation. The problems with this metallic stents however are that they have proven to be thrombogenic and can cause an acute thrombotic occlusion of the treated blood vessel. On the other hand, it appeared that through the inplantation of a metal stent in a blood vessel, the body can react with an inflammatory reaction whereby restenosis within the stent can occur. By covering these endovascular protheses with amphiphylic polyurethanes, we succeeded in significantly limiting both the problem of trombogenecity as well as the problem of reactive hyperproliferative response.
Amphiphilic polyurethanes were synthesized starting from amphiphilic polyester diols on the basis of ethylene oxide and proylene oxide. By reaction with a diisocyanate and a chain lengthener (butanediol), a thermoplastic polyurethane is finally obtained. By the appropriate choice of a) the polyesterdiol, especially the proportion of ethyleneoxide/propyleneoxide, and b) the molecular weight of the diol, the bio- and blood compatibility can be optimized. Furthermore the kind of sterilisation of polyurethane-coated devices turned out to be very critical. We used certain amounts of gamma radiation which resulted in the formation of further crossbridging of the polymer leading to a more stable and more elastic polymer which is critical during the stent deployment. The resulting polymers turned out to be very stable when inplanted in human or animal tissues or blood vessels. Furthermore they did not provoke any inflammatory reaction.
Furthermore we were able to load these polyurethanes with medicines, which were released slowly at the polymer implantation side. These medicines are used to further decrease the thrombogenecity of the stents (heparin, hirudin, streptokinase, urokinase, tpa and other anticoagulants) and

to inhibit the inflammatory reaction caused by the stent (corticosteroids, antimitotics, angiopeptin and other antiinflammatoy drugs.) Using methylprednisolone loaded polyurethane coated stents we were able to block totally the stent restenosis in a pig coronary model.

APPLICATION POSSIBILITES OF THE SYSTEM

1. Treatment of blood vessel stenosis in humans and animals.
2. Treatment of complications occurring during other treatment methods of blood vessel stenosis.
3. Treatment of complications occurring during diagnostic procedures.
4. Coating of prosteses, wires, and catheters introduced for medical purposes.